REMARKS

By this Amendment claim 7 has been canceled.

In the outstanding final Office Action the examiner has rejected claims 1-4, 7, 9, 10, 12-14, 16 and 22 under 35 U.S.C. 103(a) as being unpatentable over Barnett et al. in view of Zecchino et al., claims 1 and 5-8 under 35 U.S.C. 103(a) as being unpatentable over Barnett et al. in view of Zecchino et al. and Wheeler et al., claims 1, 10 and 11 under 35 U.S.C. 103(a) as being unpatentable over Barnett et al. in view of Zecchino et al. and Leigh et al., and claims 1 and 17-21 under 35 U.S.C. 103(a) as being unpatentable over Barnett et al. in view of Zecchino et al. and Metziger et al.

The applicants vigorously disagree with these rejections.

Claim 1 of the present application is directed to an oral drug delivery system which comprises a continuous hydrophilic phase, a pharmaceutically acceptable oil which forms a discontinuous phase and has a drug dissolved or dispersed therein, and a surfactant to enable the formation of a stable biliquid foam. The examiner has simply stated that Barnett et al. disclose the preparation of drug delivery systems in polyaphron foam. However, this summary is incomplete since it does not explain the fundamental differences between claim 1 of the present application and the disclosure of Barnett et al. It is an important aspect of the drug delivery system of claim 1 of the present application that the drug is a poorly water-soluble drug. This is defined on page 5, lines 18 to

20 of the application as meaning a drug which dissolves in water in an amount of less than 1% by weight and this limitation is included in claim 1. In other words, the drug delivery system contains polyaphrons in which the poorly water-soluble drug is present in the oil discontinuous phase, and remains in that phase. The drug cannot escape into the continuous hydrophilic phase since it is not soluble in that phase.

Furthermore, because the continuous hydrophilic phase makes up a maximum of 20 wt.% of the oral drug delivery system, the system has a good compatibility with gelatin, enabling the drug formulation to be capsulated in hard or soft gelatin capsules (see page 4, lines 20 to 28 and claim 19). The oral drug delivery system of the present invention, therefore, effectively deals with the problem of including poorly water-soluble drugs in drug delivery systems which have good bioavailability of the drug and which are compatible with gelatin capsules.

This should be contrasted with the disclosure of Barnett et al., which is already acknowledged as prior art on page 3, line 31 to page 4, line 13 of the present application. Barnett et al. describe a polyaphron composition having a continuous phase and a disperse phase in which the drug is carried in the disperse phase (see the Abstract). However, the drug must be water-soluble. This is because the invention of Barnett et al. is to allow the drug to be transferred easily into an aqueous medium (see column 1, lines 46 to 50 and claim 1). Thus, there are a number of fundamental differences between the compositions of Barnett et al. and

those of claim 1 of the present application. In particular, the generic reference to drugs in Barnett el al., and the specific disclosure of scopolamine, are for drugs which are water-soluble, otherwise they could not be transferred into the aqueous medium. Claim 1 of the present application requires the drug to be poorly water-soluble as indicated above. Furthermore, in Barnett et al. there is no disclosure of the amount of continuous hydrophilic phase and pharmaceutically acceptable oil. The preparation method given in column 2 of Barnett et al. does not indicate the amount of water used. Regardless of this, however, the passage on column 2, lines 47 to 51 clearly indicates that, for the partitioning, 40 ml of polyaphrons was partitioned against 100 ml of distilled water. Clearly the amount of continuous hydrophilic phase in the total composition is significantly more than the maximum of 20 wt.% allowed in claim 1 of the present application. Because of the amount of water which is present the compositions of Barnett et al., they cannot be used in gelatin capsules since the water in the composition would dissolve the capsules.

The objective problem to be solved by the present invention is as set out in the first paragraph of the present application, namely to provide a drug delivery system for the oral administration of lipophilic poorly water-soluble drugs which can be used in immediate release dosage forms. In other words, the problem is to provide a composition which can be incorporated into immediate release dosage forms, such as gelatin

capsules, and which enables a poorly water-soluble drug to have increased and immediate bioavailability.

Clearly, Barnett et al. do not teach one of ordinary skill in the art how to achieve this since, as indicated above, Barnett et al. is only concerned with water-soluble drugs. Furthermore, it does not mention the possibility of incorporating the composition in a unit-dosage form. Indeed, one of ordinary skill in the art reading Barnett et al. would readily understand that the compositions are not suitable for use in gelatin capsules since the large amount of water present in the compositions would dissolve the gelatin. It would not be obvious to one of ordinary skill in the art to reduce the amount of water in the compositions described in Barnett et al. since the water is required for the invention of Barnett et al., namely to transfer a drug contained within a polyaphron into the surrounding medium.

Similarly, Zecchino et al. is not relevant. Zecchino et al. describe gelled aqueous cosmetic compositions. This patent is directed to gels for use in skin treatment. Although the gels described in this patent may be used as hair care products (see page 6, first paragraph), there is no suggestion of the use of biliquid foams for the oral administration of drugs. Accordingly, it would not be obvious to combine the teaching of Zecchino et al. with Barnett et al. In fact, these patents lie in entirely different technical fields. The examiner has suggested that both of these patents are in the field of pharmaceuticals, therefore the person of

ordinary skill would easily combine them. This is not the case. The field of oral administration of drugs is very different to that of dermal treatment. Zecchino et al. only teach that the composition disclosed therein may contain pharmaceutical compositions intended for topical use (see page 6). It is silent on oral compositions. Moreover, the person of ordinary skill would know that the compositions described in Zecchino et al. would not be suitable for oral administration. Thus, in contrast to combining the teaching of these patents, the person of ordinary skill would not consider Zecchino et al. to be relevant to the problem at hand. Accordingly, it would not be obvious to combine the subject matter of claim 1 in the light of Barnett et al., and Zecchino et al. (and Reference U).

Even if the person of ordinary skill did combine Barnett et al. and Zecchino et al., he would not arrive at the present invention. Barnett et al. only disclose the presence of scopolamine in the aqueous phase. Zecchino et al. is silent on where in the composition the active agent is contained. Indeed, in the only example, caffeine (a drug) is present in phase II. The biliquid foam itself, which comprises 60% of the composition, does not contain any pharmaceutical active agent. Accordingly, the person of ordinary skill would not consider combining these documents when looking to provide a drug delivery system for the oral administration of lipophilic poorly water-soluble drugs which can be used in immediate

release dosage forms. Moreover, even if he did, he would not arrive at the present invention.

Thus, it would not be obvious to arrive at the present invention in the light of Barnett et al., Zecchino et al. and Reference U. Reference U is silent on biliquid foams and poorly water soluble drugs. It is therefore submitted that this document adds nothing further to the teaching of the person of ordinary skill.

The examiner has further suggested that the present invention would be obvious if the teaching of Barnett et al. was combined with that of Zecchino et al. and Wheeler. It is submitted that this is not the case.

Wheeler is directed to a gel and/or hair conditioning aqueous gel comprising a biliquid foam. It adds nothing to lead the person of ordinary skill to the present invention. There is no disclosure in this patent of a poorly-water soluble drug being dissolved in the pharmaceutically acceptable oil of a biliquid foam. Nor is there any disclosure of an oral drug delivery system. This patent is directed to gels for topical application- see the abstract which states that the biliquid foam comprises a dispersion of oil droplets in an aqueous medium stabilized by only a small amount of surfactant, thus keeping the level of skin irritation low. Moreover, see page 3, second full paragraph. The person of ordinary skill would not look to combine these documents when looking to provide a drug delivery system for the oral administration of lipophilic poorly water-

soluble drugs which can be used in immediate release dosage forms, and even if he did, he would not arrive at the present invention.

Furthermore, it would not be obvious to arrive at the present invention if Barnett et al. and Zecchino et al. were combined with Leigh et al. As previously described, Barnett et al. only disclose the presence of water soluble drugs in biliquid foams. There is no disclosure or suggestion of the required component percentages as recited in claim 1. Nor is there any disclosure of a poorly water-soluble drug. Zecchino et al. is silent on oral compositions. Moreover, Zecchino et al. is silent on poorly water soluble drugs. Accordingly, for the reasons outlined above, the person of ordinary would not combine these patents to arrive at the present invention. Leigh et al. disclose a substantially homogenous composition for human administration of a biologically active lipophilic compound dissolved in or associated with at least one micelle-forming liquid (see abstract). Thus, contrary to teaching towards the present invention, Leigh et al. is silent on biliquid foams, and instead teaches the use of micelle-forming liquids to solubilise poorly water soluble drugs. Thus, it would not be obvious to arrive at the present invention in the light of these patents. Instead, the person of ordinary skill would be taught towards forming a micelle-containing structure.

The examiner has further suggested that it would be obvious to arrive at the present invention if the teaching of Barnett et al. was combined with that of Zecchino et al. and Metziger et al. It is submitted that this is not the case for the reasons outlined below.

Metziger et al. disclose oral compositions for oral administration containing a medicinal product which is insoluble or sparingly soluble in water and oils and which is selected from diacerein, rhein and one of their pharmaceutically active salts (see the abstract). In particular, Metziger et al. describe that the pharmaceutical composition comprises a liquid support oil, a suspension agent, a homogenizing agent, a surfactant, and one or more pharmaceutically acceptable expedients or supports (see claim 1). The composition may be in the form of soft or hard gelatin capsules (see column 3, lines 12 to 17). Metziger et al. teach that the composition preferably comprises from between 10 and 15% by weight of surfactant relative to the total weight of the components of the active principle. Examples 1, 2 and 3 have 17%, 17%, and 13% by weight of surfactant relative to the total weight of the components of the active principle. The high levels of surfactant are necessary to solubilize the active agent in the oil. However, it is known that compositions comprising high levels of surfactant are potentially harmful on the intestinal wall. Moreover, the high levels of surfactant adds to cost and complexity of the formulation (see, for example, page 2, lines 25 to 30 of the present application). Thus, when looking to provide an improved drug

delivery system it would not be obvious to look to Metziger et al. Even if the person of ordinary skill did combine the teachings of these patents, he would not arrive at the present invention, and in particular would not arrive at a composition comprising a poorly water-insoluble drug dissolved in the pharmaceutically acceptable oil wherein the biliquid foam has only from 0.5 to 5% by weight of a surfactant. Accordingly, it would not be obvious to arrive at the present invention in the light of the cited prior art.

Favorable evaluation of the presented claims is requested.

Respectfully submitted,

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